changes in response to coronary ESC perfusion, including declines in CF, HR, LVP, +dp/dtmax, and –dp/dtmax, with increased ESC perfusion rates. However, the magnitude of these parameters differed between the two mouse strains. At less than 10^6 cells/ml/min, the percent decline of these parameters in wild type hearts appeared significantly greater ($p<0.05$) than those of apoE-/-: CF 15.2% in wild type vs. 10% in apoE-/-, HR 19% vs. 7%, LVP 9% vs. 6%, +dp/dtmax 11% vs. 8%, and –dp/dtmax 24% vs. 11%. Increasing the perfusion rates up to $5x10^6$ cells/ml/min led to further deterioration of the heart functions but the apoE-/- hearts remained lower levels of the parameter declines. Histopathological analysis showed the presence of numerous ESC in microcirculation as well as in the extravascular tissue.

Conclusions: Perfusion with ESC through coronary arteries causes concentration-dependent changes in heart function. Compared to wild type controls, the hearts of apoE-/- mice which underwent atherosclerosis-related chronic ischemia appeared to be better tolerant to high ESC perfusion.

1011-109 The Mitochondrial Metabolic Phenotype and Mouse Strain Influence Isoproterenol-Induced Cardiac Hypertrophy

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Introduction We previously described a novel model of isoproterenol (ISO)-induced hypertrophy in which A/J mice exhibit greater cardiac hypertrophy than B6 mice. The objective of this study was to determine the relation between this variable hypertrophic response and the mitochondrial metabolic phenotype.

Methods 39 male mice (19 A/J, 20 B6) received randomly either ISO (100 mg/kg, sc) or vehicle daily for five days. Hearts were assayed for the genomically-expressed mitochondrial enzymes pyruvate dehydrogenase (PDH), medium chain acyl-CoA dehydrogenase (MCAD), carnitine palmitoyl transferase I (CPT-I) and citrate synthase activities. Nine consomic B6.AM mice (B6 containing mitochondrial DNA from A/J) were also studied.

Results ISO-treated A/J mice displayed a greater increase in gravimetric heart/body weight (vs. vehicle) than ISO-treated B6 (24% vs. 3%, respectively, $p<0.001$). Enzyme activities were greater in vehicle-treated B6 than A/J mice (Table). ISO administration reduced active PDH activity (PDHa) in B6 mice by 47% ($p<0.001$), with no significant change in A/J. The hypertrophic response and basal and stimulated enzyme activites were similar in B6.AM and B6 mice.

Conclusions 1) Compared to A/J, B6 mice demonstrate less ISO-induced cardiac hypertrophy, but greater activity of fatty acid and carbohydrate oxidative enzymes. 2) ISO-induced hypertrophy reduces myocardial PDH in a strain-dependent manner. 3) These mitochondrial enzyme activities are not influenced by mitochondrial DNA.

Data are mean ± SEM. * $p<0.01$ B6 vs. A/J by ANOVA. † $p<0.001$ ISO vs. vehicle by t-test.

	A/J vehicle	B6 vehicle	A/J ISO	B6 ISO
Citrate synthase (µmol/min/gww)	59 ± 4	171 ± 5 *	56 ± 3	163 ± 6
MCAD (µmol/min/gww)	10.4 ± 1.1	11.7 ± 0.9 *	8.9 ± 0.9	13.2 ± 0.9
CPT-1 (µmol/min/gww)	1.7 ± 0.1	2.4 ± 0.2 *	1.5 ± 0.1	2.4 ± 0.2
PDH active (U/gww)	2.2 ± 0.4	4.8 ± 0.5 *	1.9 ± 0.3	2.5 ± 0.3 †

1011-110 The HNO/Nitric Oxide Donor Angeli's Salt Enhances Myocyte Contractility in a PKA-Dependent Manner

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Background: Nitroxyl anion (HNO/NO^-) donors exert similar positive inotropic/lusitropic effects in normal and failing hearts *in vivo* that are not reproduced by NO/nitrate donors. These effects are partly linked to calcitonin gene-related peptide (CGRP) release. We hypothesize that the HNO/NO^- donor Angeli's Salt (AS) has a direct positive inotropic effect on myocyte contractility.

Methods: Cardiac myocytes were isolated from wild type 1-4 month old mice, suspended in Tyrode's solution (1.8 mM calcium) and field stimulated at 0.5 Hz at 23°C. Sarcomere shortening (SS) was assessed by real-time image analysis, and Ca^{2+} transients from Indo-1 fluorescence. Data are presented at steady-state (10 minutes AS infusion).

Results: AS induced a dose-dependent inotropic response (SS: +17±3% at 0.1 mM, n=5; +28±7% at 0.25 mM, n=9; +89±12% at 0.5 mM, n=8; +135±21% at 1 mM, n=11; all $p<0.01$ versus baseline). Peak Ca^{2+} transients increased +18±7% at 0.25 mM ($p=0.05$, n=5). To test a role of Protein Kinase A (PKA) stimulation by AS, experiments were repeated in the presence of the PKA-inhibitor H89 (5 µM). AS-induced inotropy was fully reversed by H89 (-100±33%) at 0.5 mM AS, and partially blunted (-74±42%) at 1 mM (both n=4). In striking contrast, 10 min infusion of the NO-donor DEA/NO at 0.05 and 0.125 mM (equivalent to 0.1 and 0.25 mM AS) reduced SS -63±6% ($p<0.001$ vs AS 0.1 mM, n=5) and -21±11% ($p=0.002$ vs AS 0.25 mM, n=8), respectively, without altering Ca^{2+} transients. Higher DEA/NO doses did not depress contractility, but yielded insignificant changes that remained well below the positive effects of AS (e.g. 33±16% at DEA/NO 0.5 mM, <20% of the AS 1 mM response, $p=0.001$, n=16).

Conclusion: The HNO/NO^- donor AS directly enhances myocyte contractility in a dose-dependent manner that differs markedly from NO-donors. AS inotropy is coupled to an increase in Ca^{2+} transients and blunted by PKA inhibition, supporting involvement of cAMP/PKA dependent signaling.

1011-111 Homocysteine Promotes Ventricular Remodeling by Induction of Apoptosis of Rabbit Cardiomyocytes and Priming the Mast Cells to Induce Interleukin-6, With Significant Inhibition by Troglitazone

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Background:
Homocysteine (HCy) has been linked to the pathophysiology of atherosclerosis, on the other hand, it has been linked to ventricular remodeling and heart failure through pro-inflammatory causes. This may occur due to direct effects on the cardiomyocytes or indirectly by involving other cells like macrophages, fibroblasts and mast cells.
Methods:
After isolating rabbit cardiomyocytes (CMs) using the standard perfusion method, we have given d,l HCy (1x 10-4 M) to the cells and at three hours we quantitated the apoptotic cells using Flow Cytometry. We used Annexin V (FITC) - Propidium Iodide method for apoptosis detection. Apoptotic cells manifest as Annexin V - FITC positive and Propidium Iodide negative, while necrotic cells manifest as Annexin V - FITC positive and PI positive. We have also given d,l HCy to Human Leukemic Mast Cells (HMC-1) with 1 ng/mL of Interleukin 1 beta (IL1b) in a dose dependent manner (10, 50 , 100 x 10-6 M). We added the Peroxisome Proliferator Activated Receptors (PPAR) gamma agonist (Troglitazone) to the cells as well (10 x10-6 M). We used ELISA technique to quantitate the amount of Interleukin 6 (IL 6) in the supernatants after 24 hours of incubation.
Results:
We found that d,l HCy induces apoptosis of CMs in the HCy group (3.0% versus 1.0 % control , p = 0.02) . On the other hand, we noticed a dose dependent increase in IL 6 concentration in response to stimulation of HMC1 cell line with a small fixed dose of IL1b and increasing doses of d,l Hcy (35 pg/mL versus 75 pg/mL , for IL1b alone versus IL1b + HCY 100x10-6 , p= 0.004). Surprisingly, adding Troglitazone to the HCy - IL1b - HMC-1 solution blunted the stimulatory response (35 pg/mL versus 15 pg/mL, p =0.045). Low concentration Troglitazone in a separate study did not kill HMC-1 cell line per flow cytometry and viability methods.
Conclusions:
HCy induces apoptosis of rabbit cardiomyocytes, and to our knowledge this is the first experiment that documents this finding . Moreover, HCy primes the mast cells to the effects of IL1b to produce IL6, this was blunted by PPAR inhibition. Apoptosis and IL6 are involved in ventricular remodeling and heart failure. Further testing is warranted to study the various effects of HCy on cardiomyocytes.

1011-112 Use of Abciximab Prior to Primary Angioplasty in ST-Segment Elevation Myocardial Infarction Results in Early Recanalization of the Infarct-Related Artery: Results of the Multicenter Randomized ReoPro-BRIDGING Study

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Background. The ReoPro-BRIDGING Austrian multicenter randomized study investigated the effect of Abciximab (ReoPro) on infarct-related artery (IRA) patency and early reperfusion prior to primary coronary intervention (pPCI).

Methods. Thirty-eight patients with ST-segment elevation AMI were treated with ReoPro 0.25 mg/kg bolus followed by 10 ug/min infusion and randomized either to start ReoPro during the organization time (66±33 min) for pPCI (Group 1, n=18) or immediately after pPCI (Group 2, n=20). Serial measurements of creatine kinase (CK), CKMB, myoglobin, and 12-lead ECG were performed at baseline as well as 2, 4, 6, 8, 10, 12, 24 and 48 h thereafter.

Results. A trend to a more rapid and higher release of cardiac enzymes was observed in patients of Group 1: rate of rise of CK 164±203 vs 127±170 U/l/min; CKmax: 922±954 vs 776±644 U/L, CKMBmax: 120±72 vs 105±85 U/l and myoglobin max. 1399±1092 vs 909±943 ng/ml (Fig.1). ST-segment resolution >50% occurred in 12 patients (67%) in Group 1 and 6 patients (30%) in Group 2 (p=0.024) before pPCI. TIMI flow 0 was observed in 6 (33%) vs 11 patients (55%) of Group 1 vs 2 (p=0.3). Corrected TIMI frame count was significantly lower (57±33 vs 76±22 frames, p=0.034) and angiographic minimal lumen diameter was larger (0.70±0.76 vs 0.29±0.39 mm, p=0.020) in patients of Group 1.

Conclusions. Use of ReoPro in the organization phase for pPCI results in early and better recanalization of the infarct-related artery prior to pPCI with a consecutive rapid release of cardiac enzymes.